K003062

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510(k) SUMMARY

SUBMITTED BY: BD Diagnostic Systems
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PREPARED: May 11, 2001

DEVICE NAME: BACTEC® MGIT™ 960 SIR Kits

PREDICATE DEVICES: Method of Proportion agar plates, REMEL TB QUAD Plates
BACTEC® 460TB SIRE Kit

INTENDED USE: The BACTEC® MGIT™ 960 SIR Kit is a rapid qualitative procedure for susceptibility testing of *Mycobacterium tuberculosis*, from culture, to streptomycin (STR), isoniazid (INH) and rifampin (RIF). The BACTEC® MGIT™ 960 STR 4.0 Kit and the BACTEC® MGIT™ 960 INH 0.4 Kit are for testing at higher drug concentrations.

The BACTEC® MGIT™ 960 susceptibility test kits are used with the BACTEC® MGIT™ 960 System.

DEVICE DESCRIPTION:

The BACTEC® MGIT™ 960 SIR susceptibility test kits are used with the BBL® Mycobacteria Growth Indicator Tube (MGIT™)-7mL. The tube is supplemented with BACTEC® MGIT™ 960 SIR Supplement enrichment and prepared with the appropriate dilutions of streptomycin, isoniazid, and rifampin as the mechanism for performing the susceptibility test.

The BACTEC® MGIT™ 960 susceptibility tests utilize a four to thirteen day testing protocol. A standardized suspension of *Mycobacterium tuberculosis* growth, from either solid or broth culture media, is prepared. An appropriate dilution is made of this suspension and 0.5 mL is inoculated into a Growth Control tube (drug-free) and tubes containing streptomycin, isoniazid, and rifampin (this is referred to as an AST Set). The test interpretation is based on growth of the *Mycobacterium tuberculosis* isolate in the Growth Control tube compared to the growth in the drug-containing tubes.

The absence of fluorescence in the drug-containing tubes as compared to the fluorescence in the Growth Control tube is indicative of susceptibility of the organism to that drug. The presence of fluorescence in the drug-containing tubes as compared to the fluorescence in the Growth Control tube is indicative of resistance of the organism to that drug.

At the completion of the susceptibility testing protocol, the instrument reports a sensitive or resistant result for each drug at the concentration(s) being tested.

DEVICE COMPARISON:

Table 1 summarizes the similarities and differences between the BACTEC® MGIT™ 960 SIR kits, the reference method and the predicate device.

Table 1: BACTEC® MGIT™ 960 SIR kits compared to Method of Proportion and BACTEC® 460TB SIRE test

	BACTEC® MGIT™ 960 SIR kits	Method of Proportion	BACTEC® 460TB SIRE test
Intended Use	Rapid qualitative procedure for susceptibility testing of *Mycobacterium tuberculosis*, from culture, to streptomycin, isoniazid and rifampin.	Susceptibility testing of *Mycobacterium tuberculosis*, from culture, to streptomycin, isoniazid and rifampin.	Qualitative susceptibility testing of *Mycobacterium tuberculosis* from culture.
Sample Type	Pure culture of *Mycobacterium tuberculosis.*	Pure culture of *Mycobacterium tuberculosis.*	Pure culture of *Mycobacterium tuberculosis.*
Sample Source	Solid or liquid mycobacteria culture medium.	Solid or liquid mycobacteria culture medium.	Solid or liquid mycobacteria culture medium.
Sample Volume	0.5 mL of organism suspension.	0.1 mL of each dilution of the organism suspension into each quadrant.	0.1 mL of organism suspension.
Growth medium	Modified Middlebrook 7H9 broth base with nutrient additives.	Middlebrook 7H10 agar with nutrient additives.	Modified Middlebrook 7H9 broth base with nutrient additives.
Incubation Temp.	Instrument incubation at 37±1.5° C.	35 ± 2° C.	37±1°C.

Table 1: (cont.'d) **BACTEC® MGIT™ 960 SIR kits compared to Method of Proportion and BACTEC® 460TB SIRE test**

	BACTEC® MGIT™ 960 SIR kits	Method of Proportion	BACTEC® 460TB SIRE test
Reactive Ingredients of Growth Medium	APPROX. COMPOSITION/1000 mL Modified Middlebrook 7H9 Broth: Disodium phosphate 2.5 g L-Asparagine 1.25 Monopotassium phosphate 1.0 Sodium glutamate 0.5 Ammonium sulfate 0.5 Sodium citrate 0.1 Magnesium sulfate 0.05 Ferric ammonium citrate 0.04 Copper sulfate 1.0 Pyroxidine 1.0 mg Zinc sulfate 1.0 Biotin 0.5 Calcium chloride 0.5 Casein peptone 1.25 g Glycerol 3.1 mL	APPROX. COMPOSITION/1000 mL Middlebrook 7H10 Agar: Glycerol 5.0 mL Monopotassium phosphate 1.5 g Dipotassium phosphate 1.5 Monosodium glutamate 0.5 Ammonium sulfate 0.5 Sodium citrate 0.4 Ferric ammonium citrate 0.04 Magnesium sulfate 25.0 mg Zinc sulfate 1.0 Copper sulfate 1.0 Pyridoxine hydrochloride 1.0 Calcium chloride 0.5 Biotin 0.5 Malachite green 0.25	APPROX. COMPOSITION/1000 mL Modified Middlebrook 7H9 Broth: Disodium phosphate 2.5 g Monopotassium phosphate 1.0 Sodium glutamate 0.5 Ammonium sulfate 0.5 Sodium citrate 0.1 Magnesium sulfate 0.05 Ferric ammonium citrate 0.04 Copper sulfate 1.0 mg Pyridoxine 1.0 Zinc sulfate 1.0 Biotin 0.5 Calcium chloride 0.5 Casein hydrolysate 0.1 g
Additional Medium Additives	Oleic Acid, Albumin, Dextrose, Catalase (BACTEC® MGIT™ SIR Supplement)	Albumin Fraction V, Dextrose, Oleic Acid, Catalase (Beef)	Albumin and Catalase

Table 1: (cont.'d) **BACTEC® MGIT™ 960 SIR kits compared to Method of Proportion and BACTEC® 460TB SIRE test**

	BACTEC® MGIT™ 960 SIR kits	Method of Proportion	BACTEC® 460TB SIRE test
Final Drug Concentrations per Tube/Quad	BACTEC® MGIT™ 960 SIR Kit Streptomycin 1.0 µg/mL Isoniazid 0.1 µg/mL Rifampin 1.0 µg/mL BACTEC® MGIT™ 960 INH 0.4 Kit Isoniazid 0.4 µg/mL BACTEC® MGIT™ 960 STR 4.0 Kit Streptomycin 4.0 µg/mL	TB QUAD I 1 – Control no drug 2 – Isoniazid† 0.2 µg/mL 3 – Isoniazid 1.0 µg/mL 4 – Rifampin† 1.0 µg/mL TB QUAD II 1 – Control no drug 2 – Ethambutol --- 3 – Streptomycin† 2.0 µg/mL 4 – Streptomycin 10.0 µg/mL	BACTEC® 460TB SIRE test Streptomycin 2.0 µg/mL Isoniazid 0.1 µg/mL Rifampin 2.0 µg/mL
Incubation length	Four to 13 day testing protocol.	Three week testing protocol.	Four to 12 day testing protocol.
Testing Method	Automated	Manual	Semi-automated
Sensor	O_2 sensitive fluorescent sensor in silicon rubber base.	None	^{14}C labeled fatty acid present in the medium.
Growth Detection	Presence/absence of fluorescence in each tube.	Visual observance of growth.	Radiometric detection of $^{14}CO_2$ liberated by microorganism growth.
Result Interpretation	Software algorithm compares signal data from Growth Control tube to each drug-containing tube in the AST Set.	Manual calculation of colony counts in the Control quadrant and each drug-containing quadrant to determine percent resistance.	Manual comparison of Growth Index values for Growth Control vial and each drug-containing vial.
Result Reported	Sensitive, Resistant or Error to each drug tested.	Sensitive or Resistant to each drug tested.	Sensitive or Resistant to each drug tested.

†CDC recommended critical concentration[1].

[1] Kent, P.T. and Kubica, G.T., 1985. Public Health Mycobacteriology, A Guide for the Level III Laboratory, US DHHS/PHS/CDC, Division of Laboratory Training and Consultation, Atlanta, GA.

SUMMARY OF PERFORMANCE DATA:

Analytical studies:

Lot Reproducibility:

Lot reproducibility was evaluated using twenty-five *M. tuberculosis* strains (to include five ATCC® strains). Each BACTEC® MGIT™ 960 SIR test at the critical drug concentrations was performed in triplicate for a total of seventy-five results per drug. Each replicate represented a separate test condition differentiated by lot of SIR drug and SIR Supplement used (three lots each).

Those strains that were determined resistant to streptomycin or isoniazid in the initial test were then tested with the high drug concentration, except the ATCC® strains. In addition to the resistant strains tested, two sensitive strains to STR (critical concentration) and two sensitive strains to INH (critical concentration) were included in the susceptibility profile test. Observed results were compared to the expected results.

The overall reproducibility for each drug at the critical concentration is 96.4% for STR, 100% for INH and 100% for RIF. The overall reproducibility for each drug at the high concentration is 96.3% for STR 4.0 and 100% for INH 0.4.

CDC Challenge Panel Testing:

The performance of the BACTEC® MGIT™ 960 SIR susceptibility test was evaluated using a panel of challenge strains obtained from the Centers for Disease Control and Prevention (CDC), GA, USA. The panel consisted of thirty strains of *M. tuberculosis* with known susceptibility patterns (using MOP). The panel was tested twice with the BACTEC® MGIT™ 960 SIR susceptibility test and both results were in agreement. The BACTEC® MGIT™ 960 SIR results were compared to the CDC expected results.

The overall agreement with CDC expected results for each drug at the critical concentration is 93.3% for STR, 100% for INH and 100% for RIF. The overall agreement with CDC expected results for each drug at the high concentration is 100% for STR 4.0 and 100% for INH 0.4.

Clinical Evaluation

The BACTEC® MGIT™ 960 SIR susceptibility test was evaluated at four geographically diverse clinical sites composed of regional reference centers and university hospital-based laboratories, including one foreign site. The BACTEC® MGIT™ 960 SIR susceptibility test was compared to the Method of Proportion (MOP) susceptibility test method.

Reproducibility Testing:

The reproducibility of the BACTEC® MGIT™ 960 SIR test was evaluated at the clinical sites using a panel of ten qualified strains, including several strains resistant to each of the drugs. The BACTEC® MGIT™ 960 SIR test results were compared to the expected results. The overall reproducibility for each drug at the critical concentration is 98.9% for STR, 99.7% for INH and 99.2% for RIF. Individual site reproducibility ranged from 97.8% to 100% for the combined critical concentration drug results. The overall reproducibility for each drug at the high concentration is 99.7% for STR 4.0 and 95.6% for INH 0.4. Individual site reproducibility ranged from 92.2% to 100% for the combined high concentration drug results.

CDC Challenge Panel Testing:

The performance of the **BACTEC MGIT** 960 SIR susceptibility test was evaluated using a panel of challenge strains obtained from the Centers for Disease Control and Prevention (CDC), GA, USA. The panel consisted of thirty strains of *M. tuberculosis* with known susceptibility patterns (using MOP) tested by each clinical site.

Table 2 shows the agreement of the **BACTEC MGIT** 960 SIR susceptibility test for each drug compared to the CDC expected results.

Table 2: CDC Challenge Panel – BACTEC MGIT 960 Clinical Site Testing

MGIT 960	Number tested	Number Correct	% Correct
STR 1.0	120	111	92.5
INH 0.1	120	119	99.2
RIF 1.0	120	120	100
STR 4.0	29*	29	100
INH 0.4	87*	82	94.3

* Only isolates resistant at critical concentrations tested at STR 4.0 and INH 0.4.

Clinical Isolate Testing:

A total of 106 clinical isolates of *M. tuberculosis* were tested with the **BACTEC MGIT** 960 SIR susceptibility test and the MOP susceptibility test. This included testing of both fresh clinical and stock isolates from both liquid and solid culture sources. This generated a total of 195 test results for the initial susceptibility test performed for each drug (critical concentration).

Table 3 presents the results from clinical isolate testing for each drug (critical concentration) from liquid source cultures. Table 4 presents the results from clinical isolate testing for each drug (critical concentration) from solid source cultures.

Table 3: Clinical Isolate Results – BACTEC MGIT 960 AST Compared to Method of Proportion from Liquid Source Cultures

DRUG	Method of Proportion			MGIT 960 AST System				
	Concen-tration	S	R	Concen-tration	Susceptible Results		Resistant Results	
					# Agreement	% Agreement (95% CI)	# Agreement	%Agreement (95% CI)
STR	2.0 µg/mL	69	27	1.0 µg/mL	62	90 (80– 96)	26	96 (81–100)
INH	0.2 µg/mL	59	37	0.1 µg/mL	57	97 (88-100)	36	97 (86-100)
RIF	1.0 µg/mL	72	24	1.0 µg/mL	71	99 (93-100)	24	100 (95-100)

All isolates with discordant BACTEC® MGIT™ 960 results were tested by MOP at two independent sites. Of the seven discordant STR resistant (R-960, S-MOP) isolates tested, three had resistant results from both sites, three had a resistant result from one of the two sites and one had susceptible results from both sites. The discordant STR susceptible (S-960, R-MOP) isolate had susceptible results from both sites. Of the two discordant INH resistant (R-960, S-MOP) isolates tested, both isolates had susceptible results from both sites. The discordant INH susceptible (S-960, R-MOP) isolate had susceptible results from both sites. The discordant RIF resistant (R-960, S-MOP) isolate had resistant results from both sites.

Table 4: Clinical Isolate Results – BACTEC MGIT 960 AST Compared to Method of Proportion from Solid Source Cultures

DRUG	Method of Proportion			MGIT 960 AST System				
					Susceptible Results		Resistant Results	
	Concentration	S	R	Concentration	# Agreement	% Agreement (95% CI)	# Agreement	%Agreement (95% CI)
STR	2.0 µg/mL	70	29	1.0 µg/mL	65	93 (84-98)	28	97 (82-100)
INH	0.2 µg/mL	63	36	0.1 µg/mL	62	98 (92-100)	35	97 (86-100)
RIF	1.0 µg/mL	70	29	1.0 µg/mL	70	100 (95-100)	26	90 (73-98)

All isolates with discordant BACTEC® MGIT™ 960 results were tested by MOP at two independent sites. Of the five discordant STR resistant (R-960, S-MOP) isolates tested, two had resistant results from both sites, two had a resistant result from one of the two sites and one had susceptible results from both sites. The discordant STR susceptible (S-960, R-MOP) isolate had resistant results from both sites. The discordant INH resistant (R-960, S-MOP) isolate had susceptible results from both sites. The discordant INH susceptible (S-960, R-MOP) isolate had resistant results from both sites. Of the three discordant RIF susceptible (S-960, R-MOP) isolates tested, all had susceptible results from both sites.

Table 5 presents the results from clinical isolate testing for streptomycin and isoniazid (high concentration) from liquid source cultures. Table 6 presents the results from clinical isolate testing for streptomycin and isoniazid (high concentration) from solid source cultures.

Table 5: Clinical Isolate Results – BACTEC MGIT 960 AST Compared to Method of Proportion from Liquid Source Cultures

DRUG	Method of Proportion			MGIT 960 AST System				
					Susceptible Results		Resistant Results	
	Concentration	S	R	Concentration	# Agreement	% Agreement (95% CI)	# Agreement	%Agreement (95% CI)
STR	10.0 µg/mL	77	19	4.0 µg/mL	73	95 (87-99)	17	90 (67-99)
INH	1.0 µg/mL	65	31	0.4 µg/mL	65	100 (95-100)	29	94 (79-99)

All isolates with discordant BACTEC® MGIT™ 960 results were tested by MOP at two independent sites. Of the four discordant STR resistant (R-960, S-MOP) isolates tested, all had susceptible results from both sites. Of the two discordant STR susceptible (S-960, R-MOP) isolates tested, one had susceptible results from both sites and one had resistant results from both sites. Of the two discordant INH susceptible (S-960, R-MOP) isolates tested, one had susceptible results from both sites and one had resistant results from both sites.

Table 6: Clinical Isolate Results – BACTEC MGIT 960 AST Compared to Method of Proportion from Solid Source Cultures

DRUG	Method of Proportion			MGIT 960 AST System				
					Susceptible Results		Resistant Results	
	Concen-tration	S	R	Concen-tration	# Agreement	% Agreement (95% CI)	# Agreement	%Agreement (95% CI)
STR	10.0 µg/mL	78	21	4.0 µg/mL	73	94 (86-98)	17	81 (58-95)
INH	1.0 µg/mL	68	31	0.4 µg/mL	68	100 (95-100)	30	97 (83-100)

All isolates with discordant BACTEC® MGIT™ 960 results were tested by MOP at two independent sites. Of the five discordant STR resistant (R-960, S-MOP) isolates tested, all had susceptible results from both sites. Of the four discordant STR susceptible (S-960, R-MOP) isolates tested, three had susceptible results from both sites and one had resistant results from both sites. The discordant INH susceptible (S-960, R-MOP) isolate had resistant results from both sites.

The overall performance data demonstrate that the BACTEC® MGIT™ 960 SIR Kit, the BACTEC® MGIT™ 960 STR 4.0 Kit and the BACTEC® MGIT™ 960 INH 0.4 Kit, used with BACTEC® MGIT™ 960 System, are substantially equivalent[2] to the Method of Proportion susceptibility test that was in use prior to May 28, 1976.

[2] The term "substantial equivalence" as used in this 510(k) notification is limited to the definition of substantial equivalence as found in the Federal Food, Drug and Cosmetic Act, as amended and as applied under 21 CFR 807, Subpart E under which a device can be marketed without pre-market approval or reclassification. A determination of substantial equivalency under this notification is not intended to have any bearing whatsoever on the resolution of patent infringement suits or any other patent matters. No statements related to, or in support of substantial equivalence herein shall be construed as an admission against interest under the US Patent Laws or their application by the courts.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUN - 6 2001

Ms. Jody J. Hoffmann
Regulatory Affairs Specialist
BD Diagnostic Systems
7 Loveton Circle
Sparks, MD 21152

Re: 510(K) Number: K003062
Trade/Device Name: BACTEC® MGIT™ 960 SIR Kits
Regulation Number: 866.1640
Regulatory Class: II
Product Code: MJA
Dated: May 11, 2001
Received: May 14, 2001

Dear Ms. Hoffmann:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

510(k) Number (if known): K003062

Device Name: BACTEC® MGIT™ 960 SIR Kit

Indications for Use:

The BACTEC® MGIT™ 960 SIR Kit is a rapid qualitative procedure for susceptibility testing of *Mycobacterium tuberculosis*, from culture, to streptomycin (STR), isoniazid (INH) and rifampin (RIF). The BACTEC® MGIT™ 960 STR 4.0 Kit and the BACTEC® MGIT™ 960 INH 0.4 Kit are for testing at higher drug concentrations.

The BACTEC® MGIT™ 960 SIR kits are used with the BACTEC® MGIT™ 960 System. The BACTEC® MGIT™ 960 SIR Kit final test concentrations are 1.0 µg/mL for streptomycin, 0.1 µg/mL for isoniazid and 1.0 µg/mL for rifampin. The BACTEC® MGIT™ 960 STR 4.0 Kit final test concentration is 4.0 µg/mL for streptomycin and the BACTEC® MGIT™ 960 INH 0.4 Kit final test concentration is 0.4 µg/mL for isoniazid.

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Concurrence of CDRH, Office of Device Evaluation (ODE)

(Division Sign-Off)
Division of Clinical Laboratory Devices

510(k) Number K003062

(Optional Format 3-10-98)